REMARKS

Reconsideration and withdrawal of the objections to and rejections of the application are respectfully requested in view of the amendments, remarks and attachment(s) herewith, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 12-39 are now pending, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

Support for claims 12-39 can be found throughout the application as originally filed, including in the original claims. No new matter is added.

Any fee occasioned by the new claims herein or any overpayment in such a fee, may be charged or credited to Deposit Account No. 50-0320.

It is submitted that the claims as originally-presented and as herein presented are patentably distinct from the references cited by the Examiner, and that these claims – the claims herewith and the claims originally-presented - are and were in full compliance with the requirements of 35 U.S.C. §112. The addition of claims herein is not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the addition of claims herein is made simply for clarification and to round out the scope of protection to which Applicants are entitled.

It is explicitly submitted that the addition of claims herein is not a narrowing of scope from the originally-presented claims, such that there should be no estoppel by the amendments herewith.

In addition, the Examiner is thanked for indicating that original claim 6 is free of the art.

New claims 13 and 14 herewith represent subject matter believed to be found free of the art in the Office Action.

Ergo, claims 13 and 14 and the claims dependent thereon should be allowable; and, it is respectfully requested that such be indicated in the next action.

II. OBJECTIONS TO THE SPECIFICATION AND CLAIMS ARE OVERCOME

The specification has been amended and claim 2 (referred to by the Examiner as page 30, line 20) has been cancelled, overcoming and/or rendering moot the formal, non-statutory objections set forth in the Office Action. Reconsideration and withdrawal of the objections to the specification are respectfully requested.

III. THE REJECTIONS UNDER §112 ARE OVERCOME

Claims 1-11 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Without any narrowing of scope, the terms that gave rise to the rejection do not appear in the claims herewith. Thus, reconsideration and withdrawal of the Section 112, second paragraph, rejection are respectfully requested.

Claims 1-11 were rejected under 35 U.S.C.§112, first paragraph, as allegedly being non-enabling. The rejection is traversed.

The instant invention is clearly enabled because a skilled artisan would readily understand how to make and use the invention directed to, *inter alia* an immunogenic preparation comprising a complex of: at least one plasmid encoding and expressing a nucleic acid molecule selected from the group consisting of open reading frame (ORF)1 of porcine circovirus type II (PCV-2), ORF2 of PCV-2, ORF1 of porcine circovirus type I (PCV-1) and ORF2 of PCV-1, and, an adjuvant which comprises a cationic lipid e.g., as set forth in claim 12, or the preparations set forth in claims 13 and 14.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988):

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted].

Id. at 1404.

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), for example: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art;

(6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Thus, the assertion in the Office Action that the instant invention, while being enabling for immunogenic preparations of ORF 1 and 2 of PCV-2 and of PCV-1 with DMRIE and DOPE and GM-CSF but not for an immunogenic preparation of ORFs 1 and 2 with carbomer or for immunogenic preparations with any porcine immunogen in the presence of DMRIE/DOPE, carbomer or porcine GM-CSF is misplaced because there is no undue experimentation to practice the claimed embodiments.

Applying *Wands* to the instant facts, it is clear that enablement exists, to wit, *inter alia*, that the quantity of experimentation necessary is low; the amount of direction or guidance presented is high; working examples are clearly present; the relative skill of those in the art is high; and the predictability of the art is also high, especially in view of the teachings in the application. Furthermore, the claims are not unduly broad.

Contrary to the allegations in the Office Action, no undue experimentation is required to practice the claimed invention, especially in view of the extensive teachings in the application and the knowledge in the art.

Initially, it is noted that the documents cited in the application are incorporated by reference into the application text. Thus, the text of the application is to be read as if each and every document cited therein is explicitly set forth. The Examiner is respectfully requested to re-read the application in this light.

It is further noted that the description and figures provide numerous plasmids. The application text describes the adjuvants in great detail at pages 7-9, including citing references for preparation of the adjuvants and providing amounts to be used in the claimed preparations.

Furthermore, Example 8 at page 19, lines 1-4 discloses the procedures for preparation of vaccinal solutions, the doses and routes of administration (see page 19, lines 11-19) and the vaccination schedule (see page 20, lines 11-19) for the vaccination of pigs with these vaccinal solutions.

More specifically these vaccinal solutions are prepared by diluting stock solutions in sterile physiological saline (0.9% NaCl). The stock solutions as disclosed in the instant specification are a solution containing the adjuvant, in particular a carbomer, in distilled water, preferably in the presence of sodium chloride, the solution obtained being at acidic pH. This

stock solution is then diluted by adding it to the required quantity (in order to obtain the desired final concentration), or a substantial part thereof, of water loaded with NaCl, preferably physiological saline (NaCl 9g/l), in one or more portions with concomitant or subsequent neutralization (pH 7.3 to 7.4), preferably with NaOH. This solution at physiological pH is then used for mixing with the plasmid DNA (see page 9, lines 10-23). The carbomer concentration of the final vaccine composition (0.01% to 2% w/v, more particularly 0.06 to 1% w/v, preferably 0.1 to 0.6% w/v) is also provided in the specification at page 9, lines 24-26.

Even further, Example 9 clearly states clearly that the DNA solutions of Example 8 can be replaced by the solutions of plasmid DNA formulated with DRIE-DOPE as disclosed in Example 9 (see page 20, lines 30-37). This replacement of one plasmid solution for another, in view of the teachings in the present application, would clearly not involve undue experimentation to one or ordinary skill in the art, more so considering that the detailed directions given in Examples 8 and 9 together with the disclosure in the specification for the specific plasmid solutions.

Further still, Example 8 discloses that the pigs were vaccinated with either plasmid pJP109 (encoding and expressing the ORF2 gene of PCV-2, see Figure 1), alone or with the mixture of the plasmids pJP109 and pJP111 (encoding and expressing the ORF1 gene of PCV-2, see Figure 2) or with the mixture of the plasmids pJP109 and pJP058 or with the mixture of the plasmids pJP109, pJP111 and pJP058 encoding and expressing the porcine GM-CSF (see Figure 5). Also, Example 10, page 24 shows that the immunogenic preparation comprising a plasmid expressing ORF-1 and ORF-2 of PCV-2 formulated with DMRIE-DOPE leads to significant reduction of the clinical symptoms, e.g., a reduction in the lesions and viral load and viral excretion in vaccinated pigs with respect to controls.

With regard to the allegation of the Office Action that the specification does not discuss any other porcine immunogen to delivered by the present method. Applicants' respectfully assert that instant specification details at page 9, line 38 to page 10, line 14 that the porcine immunogen can be selected from:

> the group consisting of the glycoproteins gB and gD of the Aujeszky's disease virus (pseudorabies virus or PRV), the haemagglutinin and the nucleoprotein of the porcine influenza virus H1N1, the haemagglutinin and the nucleoprotein of the porcine influenza virus H3N2, the ORF5 and ORF3 genes of the PRRS virus of the Lelystad and USA strains, the VP2 protein of the porcine parvovirus, the E1 and E2 proteins of the hog cholera virus (HCV), the deleted apxI, apxII and

apxIII genes from *Actinobacillus pleuropneumoniae* (see for the plasmids for example WO-A-9803658).

Again, note that the documents cited in the present application are incorporated by reference into the present application, such that by citing WO-A-9803658, the application teaches plasmids that encode and express the additional porcine immunogens.

Further, contrary to the allegations in the Office Action that the specification does not provide any direction for which immunogens will be used, it is noted that extensive direction has been provided in the Examples with regard to the procedures for preparation of vaccinal solutions (see page 19, lines 1-4), the doses and routes of administration (see page 19, lines 11-19) and the vaccination schedule (see page 20, lines 11-19). These procedures are easily followed by one of skill in the art and can be easily extrapolated to a plasmid or mixture of plasmids encoding and expressing any porcine immunogen with undue experimentation.

With regard to the question of protective immunity of immunogenic preparations comprising other porcine immunogens, the claimed immunogenic preparations are only for eliciting an immunological response. Thus, the claimed preparations need not be effective as a treatment for infected pigs; and, the claimed preparations need not elicit a protective immune response.

However, preparations, within the claim recitations that are effective as treatment or that elicit a protective immune response are not excluded from the claims, i.e., the claims do not exclude immunological preparations that also are effective as treatment or that elicit a protective immune response and no such exclusion is intended by the amendments and remarks herewith; the amendments and remarks are made without prejudice, without admission, without surrender of subject matter, and without any estoppel as to equivalents, especially as they are only in reply to formal, Section 112 matters.

Simply, the claims employ the term "[i]mmunogenic preparation, e.g., in accordance with pages 6-7 of the present application. An immunogenic preparation is understood as eliciting an immunogenic response. That response can be – but need not be – preventive, protective or prophylactic. Eliciting an immunogenic response is *per se* known to be useful, e.g., for eliciting antibodies, or for reducing symptoms, etc., or for preventing or protecting against illness.

However, the utility of the instant invention is not limited to the utility of a vaccine; that is, the term "[i]mmunogenic preparation" encompasses "vaccines" but is not limited to vaccines.

Hence, the Examiner, it is respectfully submitted, should not be looking for a protective response or vaccine use for all embodiments within the claims.

With regard to the reliance of the Examiner on a number of articles to show an alleged lack of enablement in the instant invention; Applicant's would like to point out that the law is very clear that an Examiner must inquire as to the knowledge of the skilled artisan at the time of filing of the application. *See In re Epstein*, 32 F.2d 1559, 1564 (Fed. Cir. 1994) ("The time relevant to the level of skill inquiry is when the application was filed[.]"); *see also*, *Graham v. John Deere*, 383 U.S. 1, 17, (1996) (finding that skill level is measured at the time the invention was made). Applicants respectfully assert that all of the articles cited by the Examiner do not reflect the knowledge in the art at the filing date of the present invention; and therefore, it is improper for the Examiner to rely on them as evidence of a lack of enablement.

The Examiner is respectfully directed to International Application WO 00 77216 A2 (copy is enclosed) which provides data regarding the immunization of pigs with ALVAC (canarypox vector) expressing either ORF13 (vCP1614) or ORF4 and ORF13 (vCP1615). ORF4 and ORF13 of the enclosed PCT correspond to ORF1 and ORF2, respectively, of the present application. Further, at page 3, last paragraph of the instant specification, and in WO 00 77216 at page 11, lines 21-24, it is clearly stated that ORF1 and ORF2 of the present application correspond to ORF4 and ORF13.

Example 9.3 of WO 00 77216 provides data that shows a significant reduction in the lymph node lesions with pigs vaccinated with ALVAC expressing ORF2 or ORF1 and ORF2, reflecting a protective effect by the vaccine. In view of the extensive teachings in the present application, there is no reason to believe that the results obtained with the canarypox vector would not be obtained by the plasmid vectors in the present invention. Therefore, a plasmid expressing ORF1 and ORF2 together is imunogenic; a plasmid expressing ORF1 is immunogenic; and a plasmid expressing ORF2 is immunogenic; and thus, there is no need to solely limit the claims to ORF1+ORF2.

Further still, the presence of GM-CSF in the claimed preparations is not essential; it is only an optional characteristic. Indeed, Example 10, experiment 2, of the present application shows that a DNA immunogenic preparation comprising a plasmid expressing ORF1 and ORF2

of PCV2, formulated with DMRIE-DOPE leads to a significant reduction of the clinical symptoms, of the lesions, of the virus loads, and of the viral excretion, in pigs immunized with that complex (in comparison with controls, after virulent challenge). There was no GM-CSF used in that experiment. Ergo, GM-CSF is not an essential feature of the present invention; only an optional characteristic. The claims need not be limited to preparations including GM-CSF.

Additionally, it is respectfully submitted that the assertion of a lack of description for the use of carbomer is unfounded. Page 9 of the present application clearly provides teachings of a formulation with carbomer and carbomer concentrations are provided (see, e.g., page 9, lines 10-26). And again, the documents cited in the present application, including at pages 7-9, are incorporated by reference into the present application.

Accordingly, when the application is read in light of the documents cited therein as appearing within the text of the present application, and, when the application is read in the light of its teachings and extensive exemplification, with the understanding that the skill in the art is high, and, when the claims are read in view of the use of the term "[i]mmunogenic preparation" (as opposed to "vaccine"), it is clear that no undue experimentation is needed to practice the claimed invention.

Consequently, reconsideration and withdrawal of the Section 112, first paragraph, rejection are warranted, and such action is respectfully requested.

IV. THE REJECTIONS UNDER 35 U.S.C. §102 ARE OVERCOME

Claims 1 and 7-9 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Okada et al. (Journal of Immunology, 1997, Vol. 159, pp. 3638-2647). Claims 1 and 11 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Meehan et al. (Journal of general virology, 1998, Vol. 79, pp. 2171-2179).

As mentioned previously, claims 13 and 14 and the claims dependent thereon reflect the subject matter found to be free of the art.

Applicants' invention in claim 12 and the claims dependent thereon, is directed to, *inter alia*, an immunogenic preparation comprising **a complex** of:, at least one plasmid encoding and expressing a nucleic acid molecule selected from the group consisting of open reading frame (ORF)1 of porcine circovirus type II (PCV-2), ORF2 of PCV-2, ORF1 of porcine circovirus type I (PCV-1) and ORF2 of PCV-1, and, an adjuvant that comprises a particular cationic lipid. The cationic lipid is advantageously N-(2-hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-

propanammonium (DMRIE). The DMRIE is advantageously coupled to a neutral lipid, such as dioleoylphosphatidylethanolamine (DOPE). The immunogenic preparation can include a porcine cytokine such as GM-CSF (or a plasmid that expresses the cytokine). None of these aspects of the invention is taught or suggested by Okada and/or Meehan.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, none of the references relied upon by the Office Action disclose, suggest or enable Applicants' invention.

Firstly, the Okada et al relates to the co-administration of a DNA vaccine directed to HIV-1 antigens with IL-2 and granulocyte/macrophage –CSF expressing plasmids with liposomes. There is no disclosure of the instantly claimed immunogenic preparations. Further, as Okada et al. fails to contain all of the elements of the claimed invention, the Section 102 rejection based thereon cannot stand.

Secondly, Meehan et al. relates solely to the characterization of the genomes of novel circoviruses isolated from North American and European pigs exhibiting wasting syndrome. The Meehan circoviruses are not plasmids. Meehan et al. fails to teach or suggest the presently claimed immunogenic preparations. Further, as Meehan et al. fails to contain all of the elements of the claimed invention, the Section 102 rejections cannot stand.

Consequently, reconsideration and withdrawal of the Section 102(b) rejection are believed to be in order; and such action is respectfully requested.

V. THE REJECTIONS UNDER 35 U.S.C. §103 ARE OVERCOME

Claims 1 and 11 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Meehan et al. in view of Okada et al. Claims 2-5 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Meehan et al. in view of Okada et al. and further in view of Felgner et al. (JBC, 1994, Vol. 269. No. 4, pp. 2550-2551). Claims 7-9 were rejected under 35 U.S.C.

§103(a) as allegedly unpatentable over Meehan et al. in view of Okada et al. and further in view of Inumaru et al. (Immunology and cell biology, 1995, vol.73, pp. 474-476). Claim 10 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Meehan et al. in view of Felgner et al. and Mumford et al. (Epidemiol. Infect., 1994, vol.112(2), pp.421-37). These rejections shall be addressed collectively.

Initially, it is noted that the rejections employ impermissible hindsight gleaned from the present application: selective picking and choosing from the reference teachings to deprecate the claimed invention. Okada, Felgner and Mumford clearly have nothing to do with PCV1 or PCV2; and, there is no teaching or suggestion that one could or should insert nucleic acid molecules from PCV1 or PCV2 into a plasmid vector; or that one would obtain a vector that indeed expresses the protein encoded by the PCV1 or PCV2 nucleic acid molecule and elicits an immunogenic response. Meehan merely relates to PCV, but fails to teach or suggest plasmids that contain and express nucleic acid molecules from PCV1 or PCV2 and which indeed elicit an immunogenic response when administered to a porcine host.

Simply, the cited document fails to disclose, suggest, or motivate a skilled artisan to practice the presently claimed invention. Just because on paper one can assert that it would be nice to make an immunogenic composition containing a plasmid, such an assertion is nothing more than the old Beach Boys song: "wouldn't it be nice if ..." Or, in other words, there is no reasonable expectation of success of an immunogenic preparation that contains a plasmid indeed eliciting an immunogenic response in the host until such a plasmid is indeed prepared and shown to be useful for its intended purpose. Combining documents in the seclusion and comfort of an office at the USPTO, it is respectfully submitted, fails to account for the numerous possibilities of failure when the plasmid is indeed constructed and then indeed administered to the porcine host; and, is thus impermissible hindsight gleaned from the present application.

The Examiner is respectfully reminded of the case law; namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine,* 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make

the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, **both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure**. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

The documents relied upon in the Office Action fail to satisfy these requirements.

There is no teaching, suggestion, or motivating recitation in Meehan et al. that would lead a skilled artisan to practice the instantly claimed invention.

Meehan et al. were simply the first to publish nucleotide sequences of circoviruses associated with wasting syndromes in pigs and does not teach or suggest an immunogenic preparation as presently claimed.

Accordingly, Meehan et al., either individually or in any combination, fails to teach or suggest the present invention.

Okada et al. also does not teach an immunogenic preparation comprising **a complex** of: at least one plasmid encoding and expressing a gene selected from the group consisting of ORF1 of PCV-2, ORF2 of PCV-2, ORF1 of PCV-1 and ORF2 of PCV-1, and, an adjuvant comprising a cationic lipid, as presently claimed

Moreover, Okada et al. relates to the administration of a HIV-1 DNA vaccine with a cationic liposome. The lipids used in the formation of cationic liposomes are completely different from cationic lipids encompassed by the present invention.

Accordingly, Okada et al., either individually or in any combination, fails to teach or suggest the present invention.

Contrary to the allegations of the Office Action that Felgner et al. discloses that cationic lipids improve DNA delivery to the cell and that therefore one would be motivated to use them as a DNA vehicle, Applicants' respectfully assert that Felgner et al. relates to **cationic liposomes** tested as to their effect on *in vitro* gene delivery of DNA, mRNA antisense oligomers, and proteins into living cells.

Felgner et al. **does not disclose the use of cationic lipids** for the delivery of an immunogenic preparation for the purpose of initiating an immune response let alone to produce improved immunogenic preparations according to the present invention.

Further Felgner et al. relates to **cationic liposomes** solely for *in vitro* transfection and expression of beta-galactosidases in COS.7 cells in culture; and, is not related to the vaccine or immunogenic field.

Present claims, e.g., claim 12 and the claims dependent thereon, specify that the plasmid expresses the PCV1 or PCV2 nucleic acid molecule *in vivo* in a porcine host; and, that the preparations contain a **complex** of the cationic lipid and the plasmid, i.e., that plasmid and cationic lipid are in the form of a complex.

The *in vivo* expression recitation distinguishes patentably from Felgner and the combinations of documents employed in the Office Action.

In regard to the latter recitation, i.e., the "complex" recitation, note that the specification at page 7, lines 16 to 21 and in Example 9 describes the formation of a complex and teaches that only gentle stirring is employed in the creating the claimed preparations. Liposomes are not formed in making the preparations of the instant invention; and, the claims a clear that liposomes are excluded.

Liposomes are multilamellar or unilamellar vesicles having a membrane portion formed of lipophilic material and an interior aqueous portion.

Due to their lamellar structure, it is expected that liposomes will allow a kind of fusion between the cell wall and the liposome and thus facilitate transfection of what is entrapped in the liposome.

In contrast, complexes of the invention are only lipid(s) loosely attached to or associated with the plasmid; not a vesicle in the sense of a liposome. Without wishing to be bound by any one particular theory, it is believed that the cationic lipid has essentially an adjuvant action, i.e., the cationic lipid enhances the immune response elicited by the plasmid – in the classic, art-known use of the term "adjuvant" – and does not enhance the delivery of the plasmid, as may the liposome in the prior art.

Accordingly, the terms "complex" and "lipid" also distinguish the claimed invention from the prior art.

Moreover, Felgner et al., alone or in combination, fails to teach or suggest the present invention.

Counter to the allegations of the Office Action, Inumaru et al. involves the cDNA cloning of porcine granulocyte-macrophage colony-stimulating factor (GM-CSF).

There is no teaching or suggestion that GM-CSF be incorporated into any type of vaccine or immunogenic preparation; and, there is no teaching or suggestion in Inumaru of the immunogenic preparations of the present invention.

Accordingly, Inumara et al., alone or in combination, fails to teach or suggest the present invention.

Consequently, reconsideration and withdrawal of the obviousness rejections under Section 103 are warranted and such action is respectfully requested.

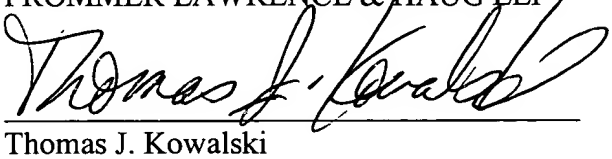
REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to any paper issuing other than a Notice of Allowance, an interview is respectfully requested; and, the Examiner is further respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for the interview.

CONCLUSION

In view of these amendments, remarks and attachment(s) herewith, the application is in condition for allowance. Early and favorable reconsideration of the application, reconsideration and withdrawal of the objections to and/or rejections of the application, and prompt issuance of a Notice of Allowance, or an interview at an early date, are earnestly solicited.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

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Appendix: Marked-Up Version To Show Changes Made

IN THE SPECIFICATION

Please amend the specification, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows:

Page 1, in the text added by the December 12, 2000 Preliminary Amendment:

[STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

Not applicable.]

Page 3, please rewrite the fourth full paragraph (the text after line 14 and before line 20), as follows:

--The subject of the present invention is plasmid constructs encoding and expressing a PCV-1 or PCV-2 immunogen, in particular the open reading frames (ORFs) 1 and/or 2 for PCV-1, and the ORFs 1 and/or 2 for PVC-2 (ORF means Open Reading Frame).--

Page 7, please rewrite the first paragraph under the formula (beginning with "in") as follows:

--in which R_1 is a saturated or unsaturated linear aliphatic radical having from 12 to 18 carbon atoms, R_2 is another aliphatic radical comprising from 2 to 3 carbon atoms, and[t] X is a hydroxyl[e ou] or amine group.--

Pages 21-22, please rewrite the paragraph that spans these pages as follows:

-- Groups of 3 or 4 piglets, caesarian-derived day 0 are placed into isolators. The piglets are vaccinated day 2 either with pJP109 alone or with pJP109 and pJP111 plasmids mixture and with a physiological solution for the control group. Each plasmid is diluted in sterile physiological solution (NaCl 0,9%) at 250 µg/ml [µl] final concentration. A 2 ml volume is injected by intramuscular route in two points of 1 ml (1 point each side of the neck). A second injection of vaccine or placebo is administered day 14. Vaccination with DNA is well tolerated by piglets and no evidence for adverse reaction to vaccination is noted. The piglets are challenged day 21 by oronasal administration of PCV-2 viral suspension, 1 ml in each nostril. After challenge piglets are weighed once a week. Rectal temperatures are recorded on days 17, 21, 22, 24, 27, 29, 31, 34, 37, 41, 44. Day 44 fecal swabs are collected from each piglet for PCV-2 shedding.

The virus is detected and quantified by quantitative PCR. Day 45 necropsies are performed and tissue samples are collected for virus isolation.--

Page 30, line one,:[CLAIMS] **We Claim:**.